

REMARKS

Reconsideration of claims 1, 6-11, 20, 22, 25-28 and 47 is respectfully requested. All of the claims are presently under Final Rejection.

In support of the rejection, the examiner relies on select statements of the Court in *KSR International v. Teleflex*, 127 S.Ct. 1727 (2007). The examiner is reminded, however, that *KSR* is not the lens through which an obviousness analysis under §103 is to be conducted. Rather, a proper §103 analysis is still governed by *Graham v. John Deere Co. of Kansas City*, 338 U.S. 1 (1966). Accordingly, the proper test is not whether the elements are known and arranged to provide an alleged predictable result, but rather, having reviewed the content of the prior art as a whole, and the scope of the patent claim, the differences between the prior art and the claims at issue are to be ascertained with the knowledge and understanding of one of ordinary skill in the art. *KSR*, 127 S.Ct. at 1734. The examiner is reminded that *KSR* is merely one case and like that of other cases is decided on its own particular set of facts as is the claims at issue here.

The statement regarding the “simple [arrangement of] old elements” relied upon by the examiner to support the rejection of all claims is not the Court’s holding in *KSR*. In fact, the statement at issue arose from a “broadbrush” understanding and conclusion of another case, *Sakaraida v. AG Pro Inc.*, 425 U.S. 273, 282 (1976).¹ Nevertheless, the examiner relies upon the statement as if it was a bright-line rule for invalidating “combination” claims of novel chemical compositions. Again, *KSR* does not establish a new or alternative framework for applying the statutory language of §103. The framework to be applied remains that of *Graham*. The Court’s reasoning in *KSR* is best summarized as follows, and not by select statements taken out of context.

Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the market place; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...

¹ In *Sakaraida*, the Court asks whether the improvement is more than the predictable use of prior art elements according to their established functions.

See *In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”). As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

KSR, 127 S.Ct. at 1740-41. The KSR Court reaffirms *Graham* and rejects the rigid application of the ‘teaching, suggestion, or motivation test (TSM test)’.²

After reminding us of the flexible approach to decide the question of obviousness, the Court provides additional comments on combination patents. Notably, the Court rejects the rigid approach taken by the examiner that all combination patents are *prima facie* obviousness. In talking directly to the examination core, the Court states

a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, *it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does*. This is so because inventions, in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some cases, is already known.

Id. at 1741. (emphasis added)

² In *KSR*, the Federal Circuit committed at least two errors; first, they failed to properly account for the nature of the problem to be solved and the common sense approach one of ordinary skill would take to solve that problem, and second, they failed to give sufficient weight to a reference that was not of record during prosecution. In both instances, the errors resulted from their rigid application of the TSM test. Particularly, in the later instance, the Federal Circuit erred because they required the prior art references to specifically address the precise problem that the patentee was trying to solve. 127 S.Ct. at 1737-38. The Court disagreed. “Throughout this Court’s engagement with the question of obviousness, our cases have set forth an expansive and flexible approach inconsistent with the way the Court of Appeals applied its TSM test here.” *Id.* at 1739 “The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents [or published patent applications].” *Id.* at 1741

The rejection of all claims is based upon an incorrect understanding of the Supreme Court's holding in *KSR*, and particularly how that holding is to be applied to the chemical arts. Inconsistent with *KSR*, the rejection puts forth a rigid, bright-line rule that "when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." By adopting such a rule the examiner commits legal error. Specifically, no reason is provided by the examiner as to why one of ordinary skill could combine the four essential components to form the claimed viscoelastic compositions. The examiner merely states that "it would have been obvious to have selected various gums from within a prior art disclosure [Singh], to arrive [at, *sic*] compositions 'yielding no more than one would expect from such an arrangement'". Final Rejection, 01/2009, page 3. Moreover, "[w]ith regard to the viscosity, percentage of quenching [claim 11], and shear-viscosities [claims 26, 27 and 47], these appear to be conventional in the art, such that their determination would have been obvious to one of ordinary skill in the art using no more than routine experimentation." Non-final Rejection, 10/2008, page 4. In essence, the examiner presents us with a rigid rule that all compositions comprising a combination of previously known components is *prima facie* obvious under §103. Applicants vehemently reject that rule and respectfully submit that the holding of *KSR* does not extend to the point the examiner wishes to go.

Provided with the proper understanding and guidance of the Court in *KSR*, we return to the claims at issue. The claims are specifically directed to viscoelastic compositions, which require specific viscosity properties not found in ophthalmic compositions formulated as eye drops. Two of the three cited references describe eye drop compositions, and the third, i.e., Gohzu et al., describes a solid-phase gel used to separate very large proteins, specifically of the immunoglobulin G subclass. The buffer solution used in the mobile phase can include one of five common types with phosphate and TRIS being preferred.

Applicants specifically request the examiner to reconsider the following grouping of claims.

Group A	1, 6, 8-10, 20 and 25 - 28
Group B	7
Group C	11
Group D	15-17
Group E	22
Group F	47

Group A: Claims 1, 6, 8-10, 20 and 25 - 28

The invention of claims 1, 6, 8-10, 20 and 25 - 28 is directed to a viscoelastic composition comprising two different viscoelastic polymers – hyaluronic acid and hydroxypropylmethyl cellulose (HPMC). The term “viscoelastic” is recited in the claims and the preamble. Therefore, there should be no question that the invention claimed must exhibit at least some viscoelastic properties recognized by one of ordinary skill in the art. It is well established that a compound or a composition and its properties are inseparable. *In re Papesch*, 315 F.2d 381 (C.C.P.A. 1963). The person of ordinary skill may be a chemist with several years of developing viscoelastic compositions or a surgeon with several years of training on the use of a viscoelastic composition during surgery. It is through the eyes of these persons of skill in which the invention needs to be viewed. Accordingly, a stated rejection under §103(a) must carefully consider who the person of ordinary skill is and armed with the art as a whole and with some understanding of his or her general knowledge in the area provide evidentiary support and sufficient reasons why that person would combine the four recited components.

In this case, Singh describes an ophthalmic composition that includes a pharmacologically active agent and a mixture of at least two gum polymers. The mixture of the gum polymers is said to increase the retention time of the active agent in the eye. See, Abstract. As Singh describes, a major problem with the administration of ophthalmic drugs is the “rapid and extensive precorneal loss caused by drainage and high tear fluid turnover.” In other words, how can one of ordinary skill develop an eye drop formulation that allows the active agent to remain in the eye for a time sufficient to

therapeutically treat a particular ocular condition? We are all familiar with placing an eye drop in the eye and experiencing the wash out affect caused by an immediate tear flow response.

To address this problem, those in the art looked to increase the viscosity of the formulations hoping that the more viscous the formulation, the more difficult it would be for the formulation to wash out. Singh describes the use of various combinations of gelling agents including gums. See, paragraphs [0008] to [0010]. Singh looked to improve upon the use of gelling agents to provide more effective ophthalmic formulations by testing various combinations. In fact, Singh lists five (5) synthetic gums, sixteen (16) natural polysaccharide gums and two (2) derivatized natural polysaccharides for a total of twenty-three (23) different gums. See, paragraph [0025]. Singh also refers to the optional addition of an “ophthalmically acceptable mucoadhesive polymer” in which hydroxypropylmethyl cellulose (HPMC) is one of ten (10) listed.

The examiner relies upon Singh for the selection of hyaluronic acid from a list of twenty-three gums and for the selection of HPMC from a list of ten “acceptable mucoadhesive polymer”. There exists no particular preference for hyaluronic acid or for the addition of the optional mucoadhesive polymer. The possible combinations, even assuming one was to add an optional mucoadhesive polymer, are 23×10 or 230 different combinations, all of which are reasoned and legally concluded by the examiner to be obvious to the person of ordinary skill. Applicants respectfully submit that the relatively large number of possible combinations alone is sufficient to defeat the examiner’s alleged *prima facie* case.

We are not, however, exactly finished with our § 103 analysis as we need to continue the “picking and choosing” to the selection of tris[hydroxymethyl]aminomethane (TRIS) and then to a nonionic osmolality agent such as a sugar alcohol. Singh lists thirteen (13) buffer components with no particular preference, one of which is TRIS. Now, the possible number of combinations is $23 \times 10 \times 13$ or 2,990 (almost 3,000 different possible combinations). Again, each of these 3,000 different compositions is reasoned and concluded by the examiner to be *prima facie* obvious to one of ordinary skill. Again, applicants respectfully disagree with this legal determination. We are still not finished.

Singh lists twelve (12) different osmolality agents, one of which is a hexahydric alcohol, i.e., mannitol. Moreover, the ionic salts are “especially preferred” over the sugar types. Yet, the examiner proposes a combination with a sugar alcohol – why? Now the potential number of combinations is $23 \times 10 \times 13 \times 12$ or 35,880 compositions – all of which are reasoned and concluded by the examiner to be *prima facie* obvious to one of ordinary skill.

Applicants must ask why one of ordinary skill having the cited references in hand, and having the knowledge of a chemist familiar with developing viscoelastic compositions, would pick and choose the claimed composition of claim 1 out of a possible 36,000? We are reminded that we are not referring to a mechanical gas pedal having a fixed or an adjustable pivot point, i.e., a 50:50 selection, as in *KSR*. Unless the examiner answers this question through reliance upon sufficient evidence and sound reasoning, a proper case of *prima facie* obviousness has not been presented. Applicants respectfully request that the rejection of claims 1, 6, 8-10, 20 and 25 - 28 be withdrawn.

Group B: Claim 7

Claim 7 is directed to a viscoelastic composition that comprises hyaluronic acid, HPMC and TRIS, all within their respective concentration ranges, and sorbitol. Olejnik, like Singh, describes an eye drop formulation, one difference being that Olejnik looks to the use of non-ionic tonicity agents such as sugar alcohols to provide an appropriate osmolality value to the formulation. Applicants wonder if Singh is said to prefer ionic osmolality agents why would one of ordinary skill look to a reference that prefers non-ionic agents. Also, given that one of ordinary skill would possess the knowledge that a widely accepted hyaluronic acid-based viscoelastic presently on the market, Healon, utilizes sodium chloride as an osmolality agent, and phosphate buffer (see, attached product description), again why would one of skill be directed to the claimed viscoelastic compositions. Applicants respectfully ask the examiner why one of ordinary skill would be motivated to diverge from a sodium chloride, phosphate buffer and find it obvious to convert to TRIS/sorbitol?

The answer to the last question is quite clear. Applicants submit that the path the examiner takes to the selection of a sugar alcohol over an ionic agent is the path of

hindsight, which we know to be improper. Applicants respectfully request that the rejection of claim 7 be withdrawn.

Group C: Claim 11

An important property of any marketable viscoelastic composition is the long-term stability or shelf-life of the composition. With respect to viscoelastic compositions, particularly, viscoelastic compositions that contain hyaluronic acid, some degradation of the hyaluronic acid, and hence, a change in the viscosity profile of the composition is expected. Applicants were confronted with the problem of stabilizing the claimed compositions. The addition of the TRIS/sorbitol enhances the stability (shelf-life) of the claimed compositions.

Each of the formulations containing tris[hydroxymethyl]aminomethane and/or sorbitol had higher free radical quenching than samples without either. Tris[hydroxymethyl]aminomethane and sorbitol individually have free-radical quenching properties. The combination of tris[hydroxymethyl]aminomethane and sorbitol have the best free-radical quenching properties.

Application page 17, bottom. The quenching profile recited in claim 11 recognizes the unique, long-term stability properties of the claimed compositions. Applicants respectfully request that the rejection of claim 7 be withdrawn.

Group D: Claims 15-17

Claims 15-17 are withdrawn from consideration, though Applicants request these claims be rejoined if claim 1 is deemed to be allowable.

Group E: Claim 22

Commercial sources of pharmaceutical grade HPMC are typically characterized as either a low molecular weight form or high molecular weight form. Applicants specifically selected the low molecular weight form to include in the claimed compositions.

The average molecular weight of the hydroxypropylmethylcellulose is a minimum of about 10 kD and a maximum of about 120 kD according to one embodiment. Typically, the average molecular weight of the hydroxypropylmethylcellulose is minimum of about 10 kD, about 12 kD or about 20 kD and a maximum of about 120 kD, about 90 kD or about 86 kD.

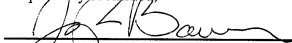
Application, page 8 (bottom) to page 9 (top). Because there is no guidance in any of the cited references to utilize the low molecular weight form over the high molecular weight form, Applicants respectively request that the rejection of claim 22 be withdrawn.

Group F: Claim 42

Claim 42 further defines the viscoelastic compositions of claim 1 by further reciting the hexahydric alcohol as sorbitol or mannitol, and the viscosity profile of claims 26 and 27. Applicants submit that claim 42 is nonobvious for the same reasons claims 1, 26 and 27 are nonobvious. The teachings and suggestions of the cited references fails to direct one of ordinary skill in the art with sufficient specificity such that one would select that one composition from the 36,000 possible combinations described in Singh. Accordingly, Applicants respectively request that the rejection of claim 42 be withdrawn.

Reconsideration of this application is respectfully requested for the reasons stated.

Respectfully submitted,



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